

Original Article

Role of Red Cell Distribution Width and Platelet Count Ratio to Predict the Severity and Outcome in Acute Pancreatitis

*Saha T¹, Mahbub I², Akhter MT³, Miah MSA⁴, Newaz AAS⁵ Akter D⁶, Hasan SMA⁷, Datta IK⁸, Chowdhury MFK⁹

Abstract

Clinical course of acute pancreatitis (AP) varies widely, its clinical features exhibit very low sensitivity for the prediction of severity of disease which is associated with high morbidity and mortality. Several single or multi parameter scoring systems have been described to evaluate the severity of AP. But sometimes, it is not clinically practicable to use these scoring systems for evaluation. This study aimed to find out the Role of Red Cell Distribution Width and Platelet Count Ratio (RPR) to predict the Severity and Outcome in AP. This prospective longitudinal study was carried out from July 2019 to July 2020, at the in-patient department of Gastrointestinal, Hepatobiliary and Pancreatic Disorders, BIRDEM General Hospital, Dhaka. Total 100 patients with AP were included for this study according to selection criteria. An informed written consent was taken from all the participants. Detail history was taken and thorough physical examination was done along with relevant laboratory investigations. Ranson's

score, Modified Glasgow score, Bedside index of severity in acute pancreatitis (BISAP), red cell distribution width and platelet count ratio (RPR) were calculated. All data were recorded and analyzed by Statistical package for social sciences (SPSS) 23. In this study 44% patients were more than 60 years with a mean age of 51.34 (± 15.45) year. More than two thirds patients were (67%) male. In mild acute pancreatitis mean value of Ranson's score, BISAP score and modified Glasgow score was 0.79 (± 0.14), 0.90 (± 0.1) and 0.80 (± 0.14) and 3.29 (± 1.16), 1.77 (± 0.46), 2.74 (± 0.69) in moderate to severe pancreatitis respectively with statistically difference were found in both severities ($p < .05$). The patients with mild pancreatitis and the patients with moderate to severe pancreatitis had significant difference ($p < .05$) between mean RDW ($14.68 \pm 1.59\%$ versus $15.51 \pm 3.27\%$), mean RPR (0.043 ± 0.06 versus $.062 \pm .002$) and platelet count (340.9 ± 841.6 cells/mm³ Versus 236.4 ± 825.4 cells/mm³). The ROC analysis of RPR in predicting severity of pancreatitis showed a cut-off value of ≥ 0.056 and diagnostic accuracy test showed sensitivity, specificity, PPV, NPV and accuracy as 63.6%, 82.2%, 81.4%, 64.9% and 72% respectively. Mean Ranson's score, BISAP score and Modified Glasgow score was 2.09 (± 1.45), 1.34 (± 0.39) and 1.83 (± 1.08) in survived patients and 5.50 (± 0.70), 4 and 3.50 (± 0.70) in dead patients with significant difference between both groups ($p < .05$). Mean RDW ($15.08 \pm 2.67\%$ Vs $17.85 \pm 0.21\%$), mean platelet count ($284.43 \pm 143 \times 10^9/L$ Vs $236.4 \pm 825.4 \times 10^9/L$) and mean RPR (0.053 ± 0.02 Vs 0.094 ± 0.005) was also significant between survived and dead patients ($p < .05$). The ROC analysis of RPR in predicting outcome showed cut-off value of ≥ 0.06 and diagnostic accuracy test showed sensitivity, specificity, PPV, NPV and accuracy as 100%, 63.27%, 5.26%, 100% and 64% respectively. Red cell distribution width and platelet count ratio (RPR) can be used as a novel biomarker to predict the severity and mortality of acute pancreatitis in very early stage.

Keywords: Red cell width distribution platelet count ratio, severity of acute pancreatitis, outcome of acute pancreatitis

INTRODUCTION

Acute Pancreatitis (AP) is defined as an acute condition presenting with abdominal pain, a threefold or greater rise in the serum levels of the pancreatic enzymes amylase or lipase, and/or characteristic findings of pancreatic

1. *Dr. Tanmoy Saha, Medical Officer, Sheikh Russel National Gastroenterology Institute and Hospital (SRNGIH), Mohakhali, Dhaka, Mobile: 0172894136. E-mail: dr.tanmoy40@gmail.com.
2. Dr. Imteaz Mahbub, Registrar, SRNGIH, Mohakhali, Dhaka
3. Dr. Md. Tuhin Akhter, Registrar, SRNGIH, Mohakhali, Dhaka.
4. Dr. Md. Shah Alam Miah, Assistant Registrar, SRNGIH, Mohakhali, Dhaka.
5. Dr. Abdullah Al Shah Newaz, Registrar, SRNGIH, Mohakhali, Dhaka.
6. Dr. Dilruba Akter, Assistant Registrar, SRNGIH, Mohakhali, Dhaka.
7. Dr. SM Ali Hasan, Assistant Registrar (Gastroenterology), Cumilla Medical College Hospital, Cumilla.
8. Dr. Indrajit Kumar Datta, Associate Professor, Dept. of GHPD, BIRDEM General Hospital.
9. Dr. Md. Fazlul Karim Chowdhury, Assistant Professor, Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University, (BSMMU), Shahbag, Dhaka.

*For correspondence

inflammation on contrast enhanced CT.¹ It is an inflammatory process in which local pancreatic injury leads to systemic inflammation through activation of cytokine cascades AP has an annual incidence of 13 to 45 per 100,000 persons and is the fifth leading cause of hospital deaths.² In the United Kingdom the incidence of AP is 150-420 cases per million and 330-430 cases per million in the United States. The clinical spectrum of AP patients varies widely ranging from mild local pancreas inflammation to severe multiple organ failure.³ Several studies indicated that the mortality rate of patients with AP is currently approximately 3.8% to 7%; in severe AP, it varies from 7% to 42%. Based on the most recent updated Atlanta classification, AP can be classified into three grades: mild acute pancreatitis (MAP), moderately severe acute pancreatitis (MSAP), and severe acute pancreatitis (SAP). MAP shows no organ failure, nor local or systemic complications. The patients' symptoms usually disappear within 1 to 2 weeks' of hospitalization with low mortality; MSAP can cause transient organ failure (duration<48h) combined with local or systemic complications; SAP is manifested by persistent organ failure (duration>48h) or death with generally poor prognosis.⁴

In acute pancreatitis, early assessment of the patient which can lead to an accurate prediction of the severity is useful for several reasons. The first well established step is the need to categorize patients at risk for complications for appropriate stratification in clinical trial. Furthermore it is important to identify the patients who are at risk for developing complications in order to be able to initiate effective management before those complications developed.⁵ Some scoring systems, such as Ranson's, Glasgow and APACHE, provide valuable clues to evaluate the severity and mortality of AP. In several studies, certain biological markers, such as elevated C-reactive protein, elevated creatinine, high blood glucose and hemoconcentration on admission, have been used to predict mortality.⁶ Complete blood count is a laboratory test frequently used in clinical practice and comprises white blood cell, red blood cell and platelet counts, and their morphological indices, such as the red cell distribution width (RDW).⁷ Red cell distribution width (RDW) is a widely used laboratory parameter for the quantification of the extent of erythrocyte anisocytosis, which is calculated by dividing SD of red blood cells (RBCs) volume by mean corpuscular volume (MCV) and multiplying by 100 to express the results as percentages, and reflects the variability of the size of the circulating erythrocytes.⁸ RDW is a traditional marker which mainly be used for the classification and differential diagnosis of anemia. Recently, more and more studies have reported that RDW, as an independent maker, has been used in

many pathophysiological conditions, such as cardiovascular diseases, pulmonary diseases, type 2 diabetes mellitus, progressive inflammatory status and even cancer, and high RDW values are associated with increased mortality in both general population and patients with the above diseases.⁹ As one of platelet indices, increased level of MPV serves as a biomarker of platelet activation. Platelets are shown to be as active players in antimicrobial host defense and the induction of inflammation and tissue repair. Once the production of platelet count is decreased, immature platelets are activated and become bigger, and the values of MPV increase. Huang, Zhang and Wu showed that patients with Persisting organ failure in acute pancreatitis showed a significantly higher value of MPV on admission.¹⁰ A recent study by Reddy et al. showed that high platelet lymphocyte ratio (PLR) value is associated with very bad prognosis and poor outcome or death in acute pancreatitis.² Another study by Chen et al. where RDW to platelet count ratio (RPR) is used to predict hepatic fibrosis stages in patients with chronic Hepatitis B¹¹. But RDW and platelet count ratio value has scarcely been investigated as, a potential biomarker of AP. Therefore, we aimed to investigate whether RPR is associated with the severity and outcome of patients with AP.

MATERIALS AND METHODS

It was a prospective observational study done in department of GastrointestinalHepatobiliary and Pancreatic disorders (GHPD) in BIRDEM General Hospital from July 2019 to July 2020. Total 100 patientswith acute pancreatitis admitted in department of gastroenterology of BIRDEM General Hospital, Dhaka was considered as study population. Patients withage less than 18 years, post ERCP pancreatitis, end stage renal disease, hematological disorders such as iron deficiency anaemia, myeloproliferative disorders, myelodysplastic syndrome and recent blood transfusion were excluded from the study. History of each patient was taken and recorded. Physical examination was done systematically. A questionnaire was filled up by the investigator which contained information about particulars of the patient including age, sex, socioeconomic condition, smoking, alcohol, drug history and other co-morbidities like diabetes mellitus, hypertension and ischemic heart disease. Presenting complains such as abdominal pain, vomiting, anorexia, jaundice was recorded. Following laboratory investigation such as serum lipase, amylase, C-reactive protein, complete blood count, serum electrolytes, serum enzymes associated with cholestasis, serum hepatic and renal function tests, bilirubin levels, fasting blood glucose, lactate

dehydrogenase, capillary gas analysis was done on admission day. Using these parameters, Ranson's score, Modified Glasgow score and BISAP score was calculated. We also calculated the red cell distribution width and platelet ratio (RPR). After measuring RPR it was compared with the usual scoring system and evaluation was done if there was any the association of RPR for prediction of the severity and outcome of acute pancreatitis. Outcome assessment was done at 5th day of follow up (in hospital mortality or survival). Statistical analysis of the study was done by computer software device as the Statistical Package for Social Science (SPSS) version 23.0. All data were interpreted with 95% Confidence Interval with accepting 5% error. In all cases, p value <.05 was considered statistically significant. The qualitative variables were expressed as frequency and percentage and the quantitative variables were expressed as mean with standard deviation. During analysis, student t test was considered to estimate the relationship or association between the variables. Sensitivity and specificity calculation was done to test by using standard formula. ROC curve was formulated to estimate the cut off value for prediction of the severity and outcome of the acute pancreatitis cases.

RESULTS

This study was conducted in department of GHPD in BIRDEM General Hospital, Dhaka. Total number of respondents was 100.

Table 1 shows majority (44%) of the respondents were ≥ 60 years old where mean age of the respondents was 51.34±15.45 years of SD. Male was predominant (67%).

Table I: Distribution of the respondents by Sociodemographic profile (n=100)

	Frequency (n)	Percentage (%)	Mean±SD
Age group			51.34±15.45
20 to 29 years	12	12	
30 to 39 years	15	15	
40 to 49 years	18	18	
50 to 59 years	11	11	
≥60 years	44	44	
Sex			
Male	67	67	
Female	33	33	

Table II shows 45% had mild pancreatitis, 39% had moderate and 16% had severe pancreatitis.

Table II: Distribution of the respondents by Severity of Acute pancreatitis (n=100)

Severity of pancreatitis	Frequency (n)	Percentage (%)
Mild	45	45
Moderate pancreatitis	39	39
Severe pancreatitis	16	16
Total	100	100

Table III shows mean value of Ranson's score, Modified Glasgow score in mild and moderate to severe acute pancreatitis patients (P<0.01). Significant difference has been found among the score in different types of severities. Beside mean RDW and Platelet count in mild pancreatitis and moderate to severe pancreatitis are also shown. Significant difference has been found with RDW, platelet and RPR in different types of severity (P<0.01).

Table III: Association between mild pancreatitis and moderate-severe pancreatitis in Ranson's score, BISAP score, Modified Glasgow score, RDW (%), Platelet count, and RPR count (n=100)

Score	Mild Pancreatitis	Moderate-severe Pancreatitis	p value
Ranson's score	0.79±0.14	3.29±1.16	*<0.01
BISAP score	0.90±0.1	1.77±0.46	*<0.01
Modified Glasgow score	0.80±0.14	2.74±0.69	*<0.01
RDW (%)	14.68±1.59	15.51±3.27	*<0.01
Platelet (109/L)	340.9±841.6	236.4±825.4	*0.006
RPR	0.043±0.06	0.062±0.02	*<0.01

*p value was determined by Independent sample t test.

The ROC analysis of RPR for the prediction of severity of acute pancreatitis showed an AUC of 0.747 (95% CI 0.650-0.843) which is statistically significant (p<0.01). A cut-off value of ≥ 0.056 showed 63.6% sensitivity and 82.2% specificity.

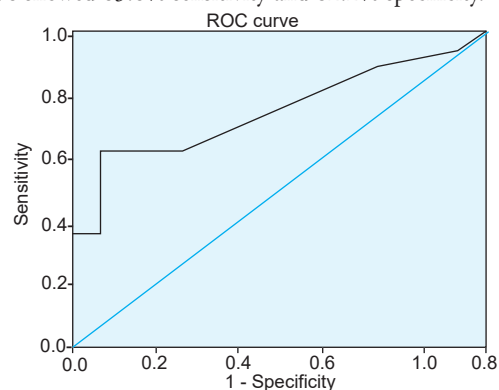


Figure I: ROC curve analysis of RPR for the prediction of acute pancreatitis

Cut off value	AUC	Std. Error	p value	95% Confidence interval	sensitivity	specificity	PPV	NPV	Accuracy
≥0.066	0.756	0.05	<0.01	0.659-0.853	50.91	93.33	90.32	60.87	70
≥0.056	0.747	0.05	<0.01	0.650-0.843	63.6	82.2	81.4	64.9	72
≥0.046	0.659	0.06	0.01	0.546-0.772	78.18	51.11	66.15	75.71	66

A cut-off value of RPR ≥ 0.056 to predict severity of acute pancreatitis showed sensitivity, specificity, PPV, NPV and accuracy as 63.6%, 82.2%, 81.4%, 64.9% and 72% accordingly.

Table IV shows 51% patients had no complications, 47% experienced complications. Mortality was 2%.

Table IV: Distribution of the respondents by Outcome (n=100)

Outcome		Frequency (n)	Percentage (%)
Survived	Pancreatitis without complication	51	51
	Pancreatitis with complication	47	47
Death		2	2
	Total	100	100

Table V shows mean RDW, mean platelet was 284.43±143 (109/L) and mean RPR was 0.053±0.02 in survivor death patients. Significant difference had been found between both groups. Beside mean Ranson's score, mean BISAP score and mean Modified Glasgow score was 1.83±1.08 in survivor patients in dead patients shows significant difference.

Table V: Association of RDW, Platelet count, RPR count, Ranson's score, BISAP score and Modified Glasgow score with mortality of patients (n=100)

Parameters	Survival	Death	p value
RDW (%)	15.08±2.67	17.85±0.21	*<0.01
Platelet (109/L)	284.43±143.70	236.4±825.4	*0.001
RPR	0.053±0.02	0.094±0.005	*<0.01
Ranson's score	2.06±1.45	5.50±0.70	*<0.01
BISAP score	1.34±0.39	4	*<0.01
Modified Glasgow score	1.83±1.08	3.50±0.70	*<0.01

*p value was determined by Independent sample t test.

The ROC analysis of RPR for the prediction of mortality in hospital due to acute pancreatitis showed an AUC of 0.969 (95% CI 0.918-1.0) which is statistically significant (p<0.01). A cut-off value of ≥ 0.06 showed 100% specificity and 63.27% sensitivity.

A cut-off value of RPR ≥ 0.06 for prediction of mortality in hospital due to acute pancreatitis showed sensitivity, specificity, PPV, NPV and accuracy as 100%, 63.27%, 5.26%, 100% and 64% accordingly.

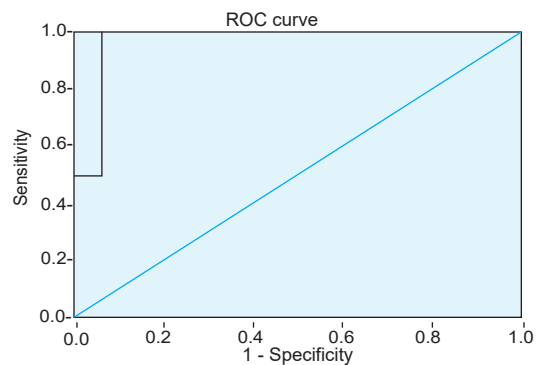


Figure 2: ROC curve analysis of RPR for the prediction of mortality in hospital

Cut off value	AUC	Std. Error	p value	95% Confidence interval	sensitivity	specificity	PPV	NPV	Accuracy
≥0.07	0.540	0.07	0.54	0.404-0.676	76.53	100	77	8.0	100
≥0.06	0.969	0.06	<0.01	0.918-1.0	63.27	100	64	5.26	100
≥0.05	0.517	0.06	0.778	0.401-0.632	40.82	100	42	3.33	100

DISCUSSION

Acute pancreatitis is one of the most common diseases of the gastrointestinal tract. Several prognostic scoring systems and biological markers have been used to predict severity and mortality in AP. However, most of them are complex. The ratio of RDW to TPC known as RPR can be evaluated as a prognostic index to know the degree of severity of SIRS and hence the outcome in acute pancreatitis.

In this study 44% respondents were equal or more than 60 years. Mean age of the respondents was 51.34±15.45. Pancreatitis often develops in people with older age because of cell and tissue changes and organs also change with increasing age. Aging organs slowly lose function. In western countries pancreatitis associated with gallstones and other causes peaks in the seventh decade beside in New York and Atlanta the peak age incidence of pancreatitis is 44 and 38 years respectively and in our country the incidence of acute pancreatitis may be differ due to lower life expectancy of Bangladeshi people.¹² In a previous study by Zhou et al., it was observed that among 406 patients' mean age was 57 years ranging from 44 to 71 years.¹³

Among the respondents of our study, 67% were male and 33% were female. Smoking, alcohol consumption is some risk factors of pancreatitis which is more common in male in Bangladeshi perspective. This can be the reason of higher number of male patients. Ahmed et al. observed out of 50 patients 32 patients were male and 18 were female where male to female ratio was 1.78:1.¹² Barad et al. did a similar type of study and observed out of 60 patients 31 were male and 29 patients were female¹⁴. Cetinkaya et al. observed among all the 102 patients 59 were female and 43 were male patients.⁷

In the current study 45% patients had mild pancreatitis, 39% had moderate and 16% had severe pancreatitis. In a previous study by Gravito et al. observed 146 (46.8%) patients had mild AP, 75 (24.0%) had moderately severe

AP and 91 (29.2%) patients had severe AP¹⁵. Barad et al. observed that among 60 patients 31 patients were having mild form of acute pancreatitis whereas 29 patients were having moderately severe or severe form of the disease¹⁴.

In our mean Ranson's score was 0.79±0.14, BISAP was 0.90±0.1 and Modified Glasgow score was 0.80±0.14 in mild pancreatitis patients beside mean Ranson's score was 3.29±1.16, BISAP was 1.77±0.46 and Modified Glasgow score was 2.74±0.69 in moderate to severe pancreatitis patients. There was significant difference found among the groups. In a previous study by Barad et al. observed mean Ranson's score was 0.774, BISAP score was 0.194 and modified Glasgow score was 0.839 in mild pancreatitis patients whereas mean Ranson's score was 4, BISAP score was 1.897 and modified Glasgow score was 3.276 in moderate to severe pancreatitis patients. Significant difference had been found between both group of patients¹⁴. Another study by Zhou et al. observed in mild pancreatitis patients mean Ranson's score was 1 and BISAP score was 1 where as in moderately severe patients mean Ranson's score was 2 and BISAP score was 2 and in severe pancreatitis patients mean Ranson's score was 4 and BISAP score was 3 that was significantly higher according to severity of patients¹³.

In this study mean RDW was 14.68±1.59, Platelet count was 340.9±841.6 and RPR was 0.043±0.06 those who had mild pancreatitis beside mean RDW was 15.51±3.27, platelet count was 236.4±825.4 and RPR was 0.062±0.02 among those who had moderate to severe pancreatitis. Significant difference had been found with RDW, platelet and RPR between severities of AP. A cut-off value of RPR ≥ 0.056 showed sensitivity, specificity, PPV, NPV and accuracy as 63.6%, 82.2%, 81.4%, 64.9% and 72% accordingly in predicting severity of acute pancreatitis. Barad et al. observed mean RPR value in mild acute pancreatitis group was 0.038 as compared to 0.068 in the severe acute pancreatitis group. In ROC curve analysis it was found that at a cut of value of 0.045 RPR has a sensitivity of around 90% and specificity of around

73% in predicting the severity of the disease¹⁴. About 51% patients had no complications, 47% had complications and 2% died according to data of our study. Zhou et al. mentioned total mortality rate was 3.45%¹³. Another study by Baradet, al. observed a total of 49 patients were cured of the disease and discharged and 11 patients died of the disease¹⁴.

In our study mean Ranson's score was 2.09 ± 1.45 , BISAP score was 1.34 ± 0.39 and Modified Glasgow score was 1.83 ± 1.08 in survivor patients beside mean Ranson's score was 5.50 ± 0.70 , BISAP score was 4 and Modified Glasgow score was 3.50 ± 0.70 in death patients. Significant difference had been found between both groups. In a previous study by Barad et al. observed mean Ranson's score was 1.653, BISAP score was 0.551 and modified Glasgow score was 1.653 in survivor patients whereas mean Ranson's score was 5.364, BISAP score was 3.091 and modified Glasgow score was 3.636 in death patients. Significant difference had been found between both groups¹⁴. Another study by Zhou et al observed in survival patients mean Ranson's score was 2 and BISAP score was 1 where as in death patients mean Ranson's score was 4 and BISAP score was 3 that was significantly higher from survival patients¹³.

In this study mean RDW was 15.08 ± 2.67 , platelet count was 284.43 ± 143.70 and RPR was 0.053 ± 0.02 in survivor beside mean RDW was 17.85 ± 0.21 , platelet was 236.4 ± 825.4 and RPR was 0.094 ± 0.005 in death patients. There was significant difference between both outcome groups with RDW, platelet count and RPR. A cut-off value of $RPR \geq 0.06$ showed sensitivity, specificity, PPV, NPV and accuracy as 100%, 63.27%, 5.26%, 100% and 64% accordingly in predicting mortality. Barad et al. found the mean RPR value was 0.044 in the survivor group and 0.089 in the death group and observed that at a cut-off value of 0.071 RPR has a sensitivity of 82% and specificity of 96% in predicting mortality in patients with acute pancreatitis¹⁴. Cetinkaya et al. observed with a cutoff value of 0.000067, RPR had a PPV 26.67%, NPV 96.39%, sensitivity 80% specificity, 70.08% in prediction of mortality⁷.

CONCLUSIONS

RPR on admission can be used to stratify the severity in acute pancreatitis patients. Patients with a high RPR value should be transferred to an intensive care unit and frequent monitoring of the condition is required in these patients.

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